The apparatus was constructed of Marinite with a 2-in. wall thickness throughout. An internal fan assured even heat distribution and markedly decreased stabilization time. A 1-mv. full-scale recorder with Disc Integrator was used. Vaporization of injected material was accomplished with a preheater with variable temperature control. Retention data are shown in Table I.

TABLE I

RETENTION TIMES FOR METHYL O-ETHYL-D-GLUCOSIDES[a]

Compound		Retention time, min.
Methyl 2,3-di-O-ethyl-D-glucoside,	α form	28
	β form	36
Methyl 2,6-di-O-ethyl-D-glucoside,	α form	44
	β form	48
Methyl 6-O-ethyl-D-glucoside		95
Methyl 3-O-ethyl-D-glucoside		106
Methyl 2-O-ethyl-D-glucoside		113

[a] Column temperature was 190°; helium pressure was 9 p.s.i.g.; 10-ft. diethylene glycol succinate (20%) column on 40–60-mesh firebrick.

Where required, paper chromatography was done in the descending manner, employing solvent systems and spray reagents described previously.[8,9]

Vinyl Starches.—The preparation and analysis of vinyl starch has been described.[2] The vinyl amylose used (D. S. 1.0) was prepared from corn amylose isolated by the Schoch procedure and having an amylose content of approximately 98% as indicated by iodine sorption.[10] The vinyl amylopectin used (D. S. 1.1) was prepared from Amioca powdered,[11] an unmodified waxy maize starch with an amylopectin content greater than 97%.

Hydrogenation of Vinyl Starch.—A solution of vinyl starch (1.0 g.) in absolute methanol (150 ml.) with 0.8 g. of 5% palladium-on-carbon catalyst[12] was hydrogenated for 70 hr. at 50° and 1800 p.s.i.g. The reaction mixture was centrifuged to remove the catalyst; evaporation of the solvent yielded 0.95 g. of product which showed no vinyl ether groups either by iodimetric or hydroxylamine hydrochloride analysis. The product, ethyl starch, was not further characterized.

Methanolysis of Ethyl Starch.—The material obtained by hydrogenation of vinyl starch was refluxed for 36 hr. in a mixture of absolute methanol (100 ml.) and concentrated hydrochloric acid (3 ml.). When cool, the reaction mixture was treated with Anion Resin CT-375[13] for 2 hr. at room temperature with stirring. The resin was removed by filtration, and the filtrate was reduced under vacuum to a clear pale yellow sirup.

Hydrolysis Procedure for Ethyl Starch or Methyl O-Ethyl-D-glucosides.—A 1–10-mg. sample of ethyl starch or methyl O-ethyl-D-glucoside was dissolved in 1.7 ml. of 72% aqueous sulfuric acid by adding the solid gradually to the acid while keeping the mixture ice-cold. After 30 min. the clear solution was diluted with water to 16-ml. total volume and refluxed for 6 hr. When cool, the reaction mixture was neutralized with Anion Resin CT-375, and the filtrate was concentrated to approximately 1 ml.

Preparation of Authentic Substances for Chromatographic Comparison. Methyl 2-O-Ethyl-α-D-glucopyranoside.—The synthesis and characterization of this compound which was in our possession has been described previously.[3]

Methyl 3-O-Ethyl-D-glucopyranoside.—The method of Glen, *et al.*,[14] was used to prepare 3-O-ethyl-D-glucose. The product, m.p. 136.5–137.5°, $[\alpha]^{24}\mathrm{D}$ +26.0° (5 min.) (water, *c* 2), was refluxed for 20 hr. with a solution of 3% anhydrous hydrogen chloride in absolute methanol. After treatment of the reaction mixture with Anion Resin CT-375 and evaporation of the solvent, a very pale yellow sirup was obtained which was not further purified or characterized.

Methyl 6-O-Ethyl-D-glucopyranoside.—The method of Ohle and Tessmar[15] was used to prepare 6-O-ethyl-D-glucose. The product, m.p. 155.5–156.5°, $[\alpha]^{26}\mathrm{D}$ +57° (water, *c* 2), was converted to the glucoside as described above and was not further purified or characterized.

Methyl 2,3-Di-*O*-ethyl-D-glucopyranoside.—The method of Croon and Flamm[5] was used to prepare 2,3-di-O-ethyl-D-glucose. The product did not crystallize, but was homogeneous by paper chromatography; it had $[\alpha]^{24}\mathrm{D}$ +51.7° (water, *c* 2). The product was converted to the glucoside as described above and was not further characterized.

Methyl 2,6-Di-O-ethyl-D-glucopyranoside.—The method of Reeves[16] was utilized in the preparation of 2,6-di-O-ethyl-D-glucose. The product,[17] m.p. 112.5–114.5°, $[\alpha]^{24}\mathrm{D}$ +54.9° (water, *c* 2), was converted to the glucoside as described above and was not further characterized.

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[8] E. L. Hirst, L. Hough, and J. K. N. Jones, *J. Chem. Soc.*, 928 (1949).

[9] R. W. Lenz and C. V. Holmberg, *Anal. Chem.*, **28**, 7 (1956).

[10] We are indebted to Dr. R. J. Dimler, Agricultural Research Service, U. S. Department of Agriculture, Peoria, Ill., for the preparation of the corn amylose.

[11] American-Maize Products Co., Roby, Ind.

[12] Englehard Industries, Inc., Newark, N. J.

[13] Eli Lilly and Co., Indianapolis, Ind.

[14] W. Glen, G. Myers, and G. Grant, *J. Chem. Soc.*, 2568 (1951).

[15] H. Ohle and K. Tessmar, *Ber.*, **71B**, 1843 (1938).

[16] R. E. Reeves, *J. Am. Chem. Soc.*, **70**, 259 (1948).

[17] Croon and Flamm[5] report the following data for this sugar: m.p. 90-92°, 114-115°; $[\alpha]^{24}\mathrm{D}$ +56° (water, *c* 2).

Reactions of α-Substituted Polynitrotoluenes. I. Synthesis of 2,2′,4,4′,6,6′-Hexanitrostilbene

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2,2′,4,4′,6,6′-Hexanitrostilbene (1) has been prepared from 2,4,6-trinitrobenzyl chloride by reaction with alcoholic potassium hydroxide. The product melts at 316°, 105° higher than the melting point for a product reported to be hexanitrostilbene, obtained from the reaction of 2,4,6-trinitrobenzyl bromide with alcoholic potassium hydroxide. That the product reported here is indeed 1 has been confirmed by molecular weight determination, elemental analyses, and by an unambiguous independent synthesis. The lower melting product obtained previously was probably 2,2′,4,4′,6,6′-hexanitrobibenzyl.

Reich, Wetter, and Widmer[1] reported a 40% yield of a crystalline product from the reaction of 2,4,6-trinitrobenzyl bromide with alcohol potassium hydroxide. Upon recrystallization from nitrobenzene this product formed pale yellow needles melting at 211°, and was assumed to be 2,2′,4,4′,6,6′-hexanitrostilbene. When this procedure was repeated in these laboratories in an effort to obtain a sample of 1 for study in a series of polynitroaromatic compounds, the results obtained were at variance with those reported by Reich. No product similar to that reported was obtained.

With 2,4,6-trinitrobenzyl chloride as the substrate in the reaction with alcoholic potassium hydroxide, however, a scintillating crystalline precipitate formed. This product crystallized from nitrobenzene in beauti-

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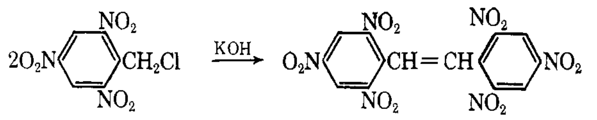
[1] S. Reich, O. Wetter, and M. Widmer, *Ber.*, **45**, 3055 (1912).



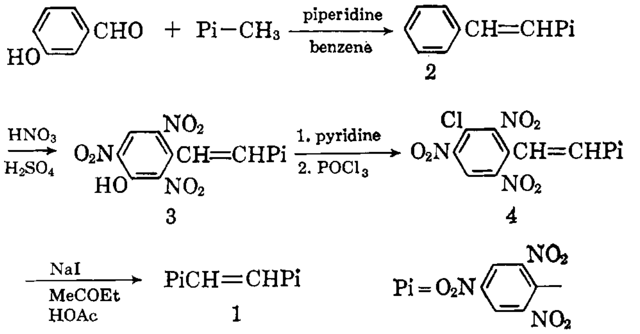
ful pale yellow needles which melted from 316 instead of 211° as reported for **1** by Reich. The melting point discrepancy might conceivably be a typographical error, but no correction was found on searching errata reported in later issues of the journal. In addition to the difference in melting point there was also a discrepancy in the solubility of the product in acetone. Reich reported ready solubility in acetone at ordinary temperatures, but the product obtained in these laboratories was only slightly soluble in hot acetone.

That the product from 2,4,6-trinitrobenzyl chloride was a stilbene and not a bibenzyl derivative was shown by the infrared spectrum which exhibited a band at 955 cm.$^{-1}$ (CH deformation in *trans* —C=C—). The measured value of the molecular weight, 448, was in excellent agreement with the calculated value, 450.3, and elemental analyses were also satisfactory. Furthermore, by analogy with other nitrobenzyl chlorides such as 4-nitrobenzyl chloride[2] and 2,4-dinitrobenzyl chloride,[3] which are known to form the corresponding stilbenes by reaction with alcoholic potassium hydroxide, **1** would be the expected product from the reaction of 2,4,6-trinitrobenzyl chloride with alcoholic base.

The above evidence pointed rather definitively to the structure **1** for the trinitrobenzyl chloride–alkali reaction product. However, owing to the apparent discrepancy between these and the previous results,[1] it was felt that an authentic sample of **1** should be prepared by an unequivocal synthetic route.

The direct nitration of stilbene was previously[4] shown to yield 2,2′,4,4′,6-pentanitrostilbene and not hexanitrostilbene. Almost as unsuccessful was the attempted condensation of trinitrobenzaldehyde with trinitrotoluene.[5] In this instance only trace amounts of a product which proved to be identical with **1** were obtained. Similarly, an oxidative coupling[6] of trinitrotoluene afforded less than 10% of a product identical with **1**. None of these procedures were considered acceptable as an unambiguous synthetic route to **1** because of the low yields obtained in each instance.

The unequivocal synthetic route took advantage of the high yield condensation reaction of trinitrotoluene with benzaldehyde.[5a] Since the 2,4,6-trinitrostilbene obtained could not be nitrated to the hexanitro derivative directly,[4] an hydroxyl group, a +M substituent, was introduced into the 3-position of the unnitrated ring to enhance the reactivity of its *ortho–para* positions in a postnitration reaction. The hydroxyl group was selected since, following nitration, it could be converted to the chloride[7] which, in turn, could be "reduced" to hydrogen according to the procedures of Blatt.[8] An over-all yield of 40–45%, with each step having a minimum yield of 65%, was obtained from the following sequence of reactions.



Condensation of 2,4,6-trinitrotoluene with 3-hydroxybenzaldehyde proceeded well in benzene solution with piperidine as catalyst to give the 3-hydroxy-2′,4′,6′-trinitrostilbene (**2**) in 90% crude yield. The crude product was nitrated to 3-hydroxy-2,2′,4,4′,6,6′-hexanitrostilbene (**3**) in 60–65% yield and the product from the nitration procedure was crystallized from acetonitrile prior to the removal of the hydroxyl group.

Removal of the hydroxyl group was achieved by modification of the procedures of Blatt[8] for the reduction of picryl chloride to trinitrobenzene. In order to apply this reduction procedure to the stilbene **3**, it was converted to the chloride **4** by treating the pyridine salt with phosphorus oxychloride.[7] The crude chloride **4**, obtained in 95% yield, was reduced directly by heating the heterogeneous mixture of **4** and sodium iodide in refluxing methyl ethyl ketone containing glacial acetic acid. By analogy with the work of Blatt, it was assumed that chloride was replaced by iodide, which in turn was reduced by hydrogen formed *in situ* from sodium iodide and acetic acid, although the iodide intermediate was not isolated. The reduction reaction afforded in 85% crude yield a light tan solid which was purified by recrystallization from nitrobenzene. This product had a melting point of 316°, which was not depressed on admixture with the product from the 2,4,6-trinitrobenzyl chloride–alkali reaction. Additionally, the two samples had superimposable infrared spectra and X-ray powder diffraction patterns.

Since the 316° product from the 2,4,6-trinitrobenzyl chloride–alkali reaction obtained in this work is, indeed, **1**, the question of the structure of Reich's[1] 211° product from the 2,4,6-trinitrobenzyl bromide–alkali reaction remains to be answered. Rather than a typographical error in the journal, a more reasonable explanation is that this product was hexanitrobibenzyl, which has a melting point of 218–220°[9] and is readily soluble in acetone at ambient temperatures. The formation of hexanitrobibenzyl under Reich's conditions is best explained by the presence of unreacted 2,4,6-trinitrotoluene in the sample of 2,4,6-trinitrobenzyl bromide.[10]

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(2) R. Walden and A. Kernbaum, *Ber.*, **23**, 1959 (1890).

(3) R. Escales, *ibid.*, **37**, 3599 (1904).

(4) F. Challenger and P. H. Clapham, *J. Chem. Soc.*, 1612 (1948).

(5) Trinitrotoluene and benzaldehyde or mononitrobenzaldehydes undergo aldol-type condensation to form the corresponding stilbenes in 50–90% yields: (a) G. Bishop and O. L. Brady, *ibid.*, **121**, 2367 (1922); (b) J. Thiele and R. Escales, *Ber.*, **34**, 2846 (1901); (c) F. Ullmann and M. Gschwind, *ibid.*, **41**, 2294 (1908).

(6) Conditions were identical with those used in preparing 2,2′,4,4′-tetranitrostilbene from 2,4-dinitrotoluene in 75% yield: A. H. Green and J. Baddiley, *J. Chem. Soc.*, **93**, 1721 (1908).

(7) M. Warman and V. I. Siele, *J. Org. Chem.*, **26**, 2997 (1961).

(8) (a) A. Blatt and E. W. Tristram, *J. Am. Chem. Soc.*, **74**, 6273 (1952); (b) A. H. Blatt and Norma Gross, *J. Org. Chem.*, **22**, 1046 (1957).

(9) W. Will [*Ber.*, **47**, 712 (1914)] reported 212° as the melting point for 2,2,,4,4′,6,6′-hexanitrobibenzyl. However, samples prepared in these laboratories melted at 218–220°.

(10) The trinitrobenzyl bromide used in Reich's work[1] was prepared by the bromination of 2,4,6-trinitrotoluene. Since trinitrotoluene and trinitrobenzyl bromide have similar solubilities in organic solvents and not widely differing melting points, contamination of the bromide by trinitrotoluene could be expected.

The mode of formation of hexanitrobibenzyl in Reich's[1] reaction, as well as the reaction path for the formation of **1** in the 2,4,6-trinitrobenzyl chloride–alkali reaction are currently under investigation and will be the subject of a forthcoming communication.

Experimental[11,12]

2,4,6-Trinitrobenzyl Bromide.—This compound was prepared by the bromination of 2,4,6-trinitrotoluene in the presence of magnesium carbonate in a sealed glass tube according to the procedure of Ganguly.[13] The yield of recrystallized material, m.p. 65°, was 62%.

2,4,6-Trinitrobenzyl Alcohol.—Hydrolysis of 2,4,6-trinitrobenzyl bromide by refluxing with water[13] gave a 63% yield of the alcohol, m.p. 100°.

2,4,6-Trinitrobenzyl Chloride.—Conversion of 2,4,6-trinitrobenzyl alcohol to the chloride was accomplished by its reaction with phosphorus pentachloride in dry chloroform.[13] A 93% yield of the chloride, m.p. 85°, was obtained.

3-Hydroxy-2′,4′,6′-trinitrostilbene (2).—To a mixture of 100 g. (0.44 mole) of 2,4,6-trinitrotoluene, 50 g. (0.41 mole) of 3-hydroxybenzaldehyde, and 750 ml. of benzene in a 1-l. round-bottomed flask was added 5 ml. of piperidine and the resulting mixture was heated to reflux using a condenser connected through a Dean–Stark trap. The reaction mixture was an homogeneous solution at reflux temperature, initially a light orange color which gradually deepened to dark brown during the heating period. After 4.5–5 hr. at reflux, when nearly the theoretical volume of water had collected in the Dean–Stark trap, *i.e.*, *ca.* 7 ml., heating was discontinued and the solution was cooled. The yellow crystalline product which formed was filtered, washed with benzene and then hexane, and dried. It weighed 135 g., or 90% of the theoretical, and melted at 156–158°. Recrystallized from methanol it formed bright yellow needles which melted at 160°.

Anal. Calcd. for $C_{14}H_9N_3O_7$: C, 50.76; H, 2.73; N, 12.68. Found: C, 51.11, 51.37; H, 2.82, 2.96; N, 12.99, 12.56.

3-Hydroxy-2,2′,4,4′,6,6′-hexanitrostilbene (3).—The addition of 100 g. of 2 to 100 ml. of 96% sulfuric acid in a 400-ml. beaker produced a dark green colored slurry. This slurry was chilled in an ice and water bath and 150 ml. of 30% oleum was added slowly with stirring, keeping the temperature of the mixture under 30°. The resulting dark red-brown viscous solution was allowed to stand at room temperature for 15 min., then heated to 85° on the steam bath and held at that temperature for 1 hr. After cooling to room temperature this solution was added slowly, with rapid stirring, during 45 min., to a mixture of 100 ml. of 70% nitric acid and 50 ml. of 96% sulfuric acid at 55–60° accompanied by the addition of 200 ml. of 70% nitric acid in 25-ml. portions. Initially the reaction mixture was an homogeneous red-brown solution but after about 5 min. a crystalline product appeared in the mixture and the color lightened to a light brown. The mixture was stirred for 10–15 min. after the addition of the stilbene–sulfuric acid solution was completed and then drowned in 2 l. of flaked ice and water. The product was filtered, washed with water, and dried. The light tan filter cake weighed 140 g. Recrystallization from 2.5 l. of acetonitrile, Celite, and Darco, yielded 87.5 g., 62% of theoretical, of fine colorless needles which melted at 274–275°. An additional 5 g. of product could be obtained by evaporating the acetonitrile filtrate to *ca.* 200 ml. and chilling. The combined yield was 65.5%.

Anal. Calcd. for $C_{14}H_6N_6O_{13}$: C, 36.06; H, 1.30; N, 18.03. Found: C, 36.53, 36.56; H, 1.60, 1.59; N, 17.33, 17.95.

Pyridine Salt of 3-Hydroxy-2,2′,4,4′,6,6′-hexanitrostilbene.—A suspension of 25 g. of 3 in 250 ml. of methanol was placed in a 1-l. creased round-bottomed flask equipped with a mechanical stirrer and heated in a water bath at 50°. To this slurry was added 10 ml. of pyridine and the mixture was stirred rapidly for 1 hr. There was an immediate formation of a yellow solid product replacing the colorless hydroxystilbene. After cooling the mixture the product was filtered, washed with methanol, and dried. It weighed 28.5 g., 97.5% of the theoretical yield. It could be used as obtained from the reaction for preparing the chloride (*vide infra*). Recrystallized from acetone it formed fine lemon yellow needles which melted at 205°.

Anal. Calcd. for $C_{19}H_{11}O_{13}N_7$: C, 41.85; H, 2.03; N, 17.98. Found: C, 42.13, 42.69; H, 2.58, 2.52; N, 17.6, 17.9.

3-Chloro-2,2′,4,4′,6,6′-hexanitrostilbene (4).—A mixture of 100 g. of the pyridine salt of 3-hydroxy-2,2′,4,4′,6,6′-hexanitrostilbene in 300 ml. of phosphorus oxychloride was heated on the steam bath. The pyridine salt dissolved to form a light yellow solution from which a colorless crystalline precipitate began to separate almost immediately. The mixture rapidly became colorless and thick with product. Heating on the steam bath was continued for 15 min., then the mixture was added slowly, with stirring, to iced water keeping the temperature under 30° by the rate of addition and addiiton of more ice. The colorless crystalline product was filtered with suction, washed with water until the washings were neutral to acid test paper, and dried. It weighed 85 g., 95% of the theoretical yield. Recrystallized from methyl ethyl ketone, it formed fine colorless needles which melted with decomposition at 250–251°.

Anal. Calcd. for $C_{14}H_5ClN_6O_{12}$: C, 34.70; H, 1.01; N, 17.3. Found: C, 34.88, 35.01; H, 1.21, 0.99; N, 16.92, 17.41.

2,2′,4,4′,6,6′-Hexanitrostilbene (1). A. From 3-Chloro-2,2′,-4,4′,6,6′-hexanitrostilbene (4)—A mixture of 100 g. of 4, 200 g. of sodium iodide, 1500 ml. of methyl ethyl ketone, and 375 ml. of glacial acetic acid was heated to reflux for 20 hr. in a creased 3-l. round-bottomed flask with mechanical stirring. Originally almost colorless, the reaction mixture rapidly became dark red-brown during heating. Complete solution was not attained at this concentration but the character of the undissolved material was observed to change rapidly to fairly large needles which, on longer heating, gradually became a very fine crystalline product. At the end of the heating period this product was filtered with suction, slurried with hot water to remove inorganic salts, washed well with methanol, and dried. It weighed 86 g., or 92% of the theoretical yield. Recrystallized from nitrobenzene, 50 g./l., it yielded 71 g. (76.5%) of pale yellow needles, m.p. 316° dec.[14]

The hexanitrostilbene (1) could also be recrystallized from dimethyl formamide but was only slightly soluble in hot acetone, methyl ethyl ketone, or glacial acetic acid.

Anal. Calcd. for $C_{14}H_6N_6O_{12}$: C, 37.33; H, 1.33; N, 18.67. Found: C, 37.24, 37.43; H, 1.83, 1.88; N, 18.52, 18.73.

The infrared spectrum[15] shows strong absorption peaks which were assigned, on the basis of the literature,[16] as follows: 1545, 1345 (asymmetric and symmetric nitro stretching); 1613, 1507 (aromatic C═C stretching); 955 (CH deformation in *trans* —C═C—); and 918 cm.$^{-1}$ (CH out-of-plane deformation in picryl group).

B. From 2,4,6-Trinitrobenzyl Chloride.—A solution of 2.6 g. (0.01 mole) of 2,4,6-trinitrobenzyl chloride in 25 ml. of methanol was heated on the steam bath and 12 ml. of methanol containing 0.01 mole of potassium hydroxide was added 2–3 drops at a time during 15 min. with vigorous shaking after each addition. A dark red color appeared after each addition. The color disappeared after shaking the first few times, but persisted after the addition of 3–4 ml. of the alkali solution. A scintillating crystalline product appeared in the reaction mixture about the time the color persisted. After the addition of the alkali solution was completed the mixture was allowed to stand 15 min. and then the product was filtered, washed well with methanol, and dried. It weighed 0.7 g., or 30% of the theoretical yield. Recrystallization from nitrobenzene yielded pale yellow needles melting at 316° dec. The infrared spectrum was superimposable on the one for A above.

C. From 2,4,6-Trinitrotoluene and 2,4,6-Trinitrobenzaldehyde.—To a solution of 0.5 g. of 2,4,6-trinitrotoluene and 0.5 g. of 2,4,6-trinitrobenzaldehyde in 5 ml. of dry acetonitrile was added 1 drop of piperidine. A dark red-brown color appeared immediately. The solution was allowed to stand at room temperature for several days, then diluted with an equal volume of

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[11] Melting points are uncorrected. Microanalyses were performed by Professor M. H. Aldridge, Department of Chemistry, American University, Washington, D. C.

[12] Caution! Many of the compounds herein described are explosive in nature. Appropriate percautions should be taken in their handling.

[13] K. L. Ganguly, *Ber.*, **58**, 708 (1925).

[14] Melting point was determined on a microscope hot stage. The iron-constantan (no. 30 wire) thermocouple was checked against the $KClO_4$ orthorhombic-cubic phase transition temperature: lit., 300°; found, 300°. Heating of the sample was started at about 300° at *ca.* 2.5°/min. Melting-decomposition was first observed at 314°.

[15] A calibrated Beckman IR-4 spectrophotometer was used to measure transmission of Fluorolube and Nujol mulls of crystalline material.

[16] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958.

methanol, and chilled. A scintillating crystalline product was filtered, washed with methanol, and recrystallized from nitrobenzene to yield only a few milligrams of pale yellow needles which were identified as 2,2′,4,4′,6,6′-hexanitrostilbene (1) by X-ray powder diffraction pattern.

Heating the reaction mixture to reflux temperature for a few minutes or for a prolonged period, or addition of a larger quantity of piperidine did not improve the yield of 1.

D. **From 2,4,6-Trinitrotoluene.**—A solution of 4.5 g. of 2,4,6-trinitrotoluene in 25 ml. of pyridine was prepared in a 300-ml. three-necked round-bottomed flask equipped with a thermometer and a mechanical stirrer. A solution of 8 g. of iodine in 75 ml. of methanol was added to the pyridine solution of TNT and the mixture was chilled to −10° in an ice–salt bath. A heavy red-gold precipitate formed which was replaced by a red-brown finely divided precipitate suspended in a blood red solution during the 0.5-hr. addition of 17 ml. of a 33% methanolic potassium hydroxide solution. After the addition of the alkali was completed the reaction mixture was stirred in the ice–salt bath for 0.5 hr., then for 15 min. after removal of the bath. The product was filtered, slurried with hot methanol and then with hot water, and dried. The dark red-brown material weighed 0.5 g., 10% of the theoretical yield. Recrystallized from nitrobenzene it yielded 0.2 g. of pale yellow needles, m.p. 315–316° dec. The X-ray powder diffraction pattern for this product was superimposable on that for A above.

Unit Cell Dimensions and Molecular Weight of 1.—X-Ray diffraction measurements on a single crystal of hexanitrostilbene showed that it had orthorhombic symmetry and the following unit cell dimensions: $a = 20.93$, $b = 5.57$, and 14.67 Å. The unit cell volume is therefore 1710 Å.^{3}. The crystal density was measured by flotation to be 1.740 g./cm.^{3}. The unit cell weight is therefore 2975 × 10^{-24} g. or 1792 molecular weight units. Since the unit cell must contain an integral number of molecules and orthorhombic symmetry indicates that the number is 2, 4, or 8, the most probable molecular weights are 896, 448, and 224. The calculated molecular weight of hexanitrostilbene, 450.3, agrees to within 1% of the observed value corresponding to 4 molecules per unit cell.

X-Ray powder diffraction pattern, interplanar spacing, Å. (relative intensity): 6.06 (23), 5.27 (37), 4.98 (58), 4.46 (27), 4.33 (13), 4.27 (12), 4.11 (20), 3.85 (97), 3.78 (100), 3.69 (73), 3.64 (60), 3.52 (25), 3.42 (8), 3.28 (15), 3.23 (17), 3.13 (48), 2.99 (28), 2.92 (27), 2.88 (15), 2.79 (37), 2.78 (35), 2.63 (47), 2.49 (17), 2.38 (17), 2.24 (13), 2.16 (5), 2.14 (3), 2.05 (10), 2.02 (8).

Acknowledgment.—This work was supported by Foundational Research funds. The author wishes to express her gratitude to other members of the Organic Chemistry Division for their assistance in this project: to H. T. Simmons for determination of crystal density, to Dr. J. R. Holden for determination of X-ray powder diffraction patterns and molecular weight by unit cell volume, to Dr. J. M. Rosen for determination of melting point, and to Drs. D. V. Sickman, M. J. Kamlet, L. A. Kaplan, and T. N. Hall for many helpful discussions and suggestions.

Pyrazines. IV. Nucleophilic Substitutions on Chloropyrazine and Alkyl Chloropyrazine N-Oxides[1a,b]

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The rapid formation of hydroxypyrazine N-oxides by the action of alkali on chloropyrazine N-oxides and alkyl chloropyrazine N-oxides, contrasted with the prolonged time required to prepare similarly the unoxidized hydroxypyrazines, suggests that the N→O group increases the reactivity of the halogen. Examples illustrating this effect are given. This activation is not noted in the preparation of ethoxypyrazine and alkyl ethoxypyrazine N-oxides by varied reagents.

Several accounts of nucleophilic substitutions on chloropyrazine and alkyl-substituted chloropyrazines have appeared in recent years.[2-6] It was of additional interest, therefore, to compare the behavior of chloropyrazine N-oxides[7] with nucleophilic reagents. The effect of the presence of N→O in this heterocyclic series has been indicated[8] by the preparation of 2-hydroxypyrazine 1-oxide in 60% yield from 2-chloropyrazine 1-oxide by heating with aqueous alkali for 2 hr. By contrast, Erickson and Spoerri[9] had to heat 2-chloropyrazine with aqueous alkali in a sealed vessel for 7 hr. (150°) to produce 2-hydroxypyrazine in comparable yield.

Attempts have been made in this laboratory to prepare 3-hydroxypyrazine 1-oxide by alkaline hydrolysis of 3-chloropyrazine 1-oxide. Although spectroscopic evidence is available for the facile formation of the desired compound within 45 min., *e.g.*, a probe sample of the reaction mixture shows absorptions at 231, 259, and 315 mμ, consistent with the predicted spectrum for this compound,[7,10] efforts to isolate good quality homogeneous material have been unsuccessful thus far. The preparation of 3-hydroxypyrazine 1-oxide has been reported by Palamidessi and Bernardi[8] by nitrous acid treatment of 3-aminopyrazine 1-oxide. Further studies are in progress.

The influence of the N→O was further illustrated by action of aqueous alkali on 3-chloro-2-methylpyrazine 1-oxide. The course of the reaction was followed spectrophotometrically and probe samples examined at intervals showed that the formation of the fully developed absorption peak at 310–315 mμ, characteristic of hydroxypyrazines, occurred within the first 15 min.

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(2) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **78**, 4071 (1956); **79**, 680 (1957).

(3) G. W. H. Cheeseman, *J. Chem. Soc.*, 242 (1960).

(4) A. Hirshberg and P. E. Spoerri, *J. Org. Chem.*, **26**, 2356 (1961).

(5) (a) H. Gainer, M. Kokorudz, and W. K. Langdon, *ibid.*, **26**, 2360 (1961); (b) W. B. Lutz, S. Lazarus, S. Klutzko, and R. I. Meltzer, *ibid.*, **29**, 415 (1964).

(6) J. D. Behun, P. Kan, P. Gibson, C. Lenk, and E. Fujiwara, *ibid.*, **26**, 4981 (1961).

(7) B. Klein, N. E. Hetman, and M. E. O'Donnell, *ibid.*, **28**, 1682 (1963).

(8) G. Palamidessi and L. Bernardi, *Gazz. chim. ital.*, **93**, 343 (1963).

(9) A. E. Erickson and P. E. Spoerri, *J. Am. Chem. Soc.*, **68**, 400 (1946).

(10) R. A. Baxter, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, 1859 (1948).